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wo89/12694.ptpn.	0

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- US Pre-Grant Publication Full-Text Database
- JPO Abstracts Database
- EPO Abstracts Database
- Derwent World Patents Index
- IBM Technical Disclosure Bulletins

Refine Search: wo89/12694.ptpn. Clear

Search History

Today's Date: 10/19/2001

DB Name	Query	Hit Count	Set Name
DWPI	wo89/12694.ptpn.	0	L7
USPT,PGPB,JPAB,EPAB,DWPI	wo89/12694.ptpn.	1	L6
USPT,PGPB,JPAB,EPAB,DWPI	(secondary adj structure) and (loop same (double adj stranded))	266	L5
USPT,PGPB,JPAB,EPAB,DWPI	loop same (double adj stranded)	829	L4
USPT,PGPB,JPAB,EPAB,DWPI	(loop same (double adj stranded))	829	L3
USPT,PGPB,JPAB,EPAB,DWPI	((secondary adj structure) same (loop and (double adj stranded)))	131	L2
DWPI	RNA and ((secondary adj structure) same (loop and (double adj stranded)))	1	L1

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***Mergent Compan Snaphot (File 556)
***Mergent Compan New Report (File 557)
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***Kompa Central/Eatern Erope (File 593)
***Kompa Canada (File 594)
***CANCERLIT (File 159)
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>>>'IALOG' not recognized as set or accession number
? b 410

    24oct01 13:33:22 User233835 Session D513.1
         $0.50    0.143 DialUnits File1
    $0.50  Estimated cost File1
    $0.05  TYMNET
    $0.55  Estimated cost this search
    $0.55  Estimated total session cost   0.143 DialUnits

File 410:Chronolog(R)  1981-2001/Oct
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      Set  Items  Description
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? set hi ;set hi

HILIGHT set on as ''
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? b 155, 5, 357, 73

       24oct01 13:33:34 User233835 Session D513.2
            $0.00    0.064 DialUnits File410
     $0.00  Estimated cost File410
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     $0.01  Estimated cost this search
     $0.56  Estimated total session cost   0.207 DialUnits

SYSTEM:OS  - DIALOG OneSearch
  File 155:MEDLINE(R)  1966-2001/Nov W3
  File   5:Biosis Previews(R)  1969-2001/Oct W3
         (c) 2001 BIOSIS
  File 357:Derwent Biotechnology Abs  1982-2001/Dec B1
         (c) 2001 Derwent Publ Ltd
*File 357: Price changes as of 1/1/01. Please see HELP RATES 357.
  File  73:EMBASE  1974-2001/Oct W2
         (c) 2001 Elsevier Science B.V.
*File  73: For information about Explode feature please
see Help News73.

      Set  Items  Description
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? s loop and ((double (w) stranded) or stem)

          121850  LOOP
          520065  DOUBLE
           92974  STRANDED
           45698  DOUBLE(W)STRANDED
          271009  STEM
      S1   10500  LOOP AND ((DOUBLE (W) STRANDED) OR STEM)
? s s1 and RNA

           10500  S1
          900435  RNA
      S2    7314  S1 AND RNA
? s s2 and interleukin

            7314  S2
          348829  INTERLEUKIN
      S3      38  S2 AND INTERLEUKIN
? rd

...completed examining records
      S4      27  RD (unique items)
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? t s4/6/1-27

4/6/1 (Item 1 from file: 155)
09989538 99058018 PMID: 9838089
Alternative splicing of mouse IL-15 is due to the use of an internal splice site in exon 5.
Dec 10 1998

4/6/2 (Item 2 from file: 155)
09621693 98049231 PMID: 9389363
Interleukin-9 in human myeloid leukemia cells.
Aug 1997

4/6/3 (Item 3 from file: 155)
09529425 97313464 PMID: 9169458
HIV-1 Tat induces the expression of the **interleukin**-6 (IL6) gene by binding to the IL6 leader **RNA** and by interacting with CAAT enhancer-binding protein beta (NF-IL6) transcription factors.
Jun 6 1997

4/6/4 (Item 4 from file: 155)
09281337 97223466 PMID: 9070287
A minimised hammerhead ribozyme with activity against **interleukin**-2 in human cells.
Feb 13 1997

4/6/5 (Item 5 from file: 155)
09269258 97211760 PMID: 9058727
CD30 ligand is frequently expressed in human hematopoietic malignancies of myeloid and lymphoid origin.
Mar 15 1997

4/6/6 (Item 6 from file: 155)
09181168 96430277 PMID: 8833403
C-kit ligand (SCF) in human multiple myeloma cells.
Feb 1996

4/6/7 (Item 7 from file: 155)
09172502 96354215 PMID: 8761952
Expression of basic helix-**loop** -helix transcription factors in explant hematopoietic progenitors.
Jun 1 1996

4/6/8 (Item 8 from file: 155)
09088756 97098461 PMID: 8943001
A cytokine mRNA-destabilizing element that is structurally and functionally distinct from A+U-rich elements.
Nov 26 1996

4/6/9 (Item 9 from file: 155)
08924337 96260074 PMID: 8661203
Transgenic animals demonstrate a role for the IL-1 receptor in regulating IL-1beta gene expression at steady-state and during the systemic stress induced by acute pancreatitis.
Jun 1996

4/6/10 (Item 10 from file: 155)

08866964 96184798 PMID: 86 5
Plasma cells induce apoptosis of pre-B cells by interacting with bone marrow stromal cells.
Apr 15 1996

4/6/11 (Item 11 from file: 155)
08425692 94229206 PMID: 7513651
A murine stromal cell line promotes the proliferation of the human factor-dependent leukemic cell line UT-7.
May 1994

4/6/12 (Item 12 from file: 155)
08182737 94286556 PMID: 8016095
The E2A and tal-1 helix-**loop**-helix proteins associate in vivo and are modulated by Id proteins during **interleukin** 6-induced myeloid differentiation.
Jun 21 1994

4/6/13 (Item 13 from file: 155)
08071017 93195347 PMID: 8450221
Platelet-derived growth factor (PDGF) activates primitive hematopoietic precursors (pre-CFCmulti) by up-regulating IL-1 in PDGF receptor-expressing macrophages.
Mar 15 1993

4/6/14 (Item 14 from file: 155)
05913867 88156918 PMID: 3258060
Autocrine generation and requirement of BSF-2/IL-6 for human multiple myelomas.
Mar 3 1988

4/6/15 (Item 15 from file: 155)
05594657 86205871 PMID: 3085085
Identification of a positive retroregulator that stabilizes mRNAs in bacteria.
May 1986

4/6/16 (Item 1 from file: 5)
12760704 BIOSIS NO.: 200000514327
p56dok-2 as a cytokine-inducible inhibitor of cell proliferation and signal transduction.
2000

4/6/17 (Item 2 from file: 5)
11647274 BIOSIS NO.: 199800429005
Transcription factor SCL is required for c-kit expression and c-kit function in hemopoietic cells.
1998

4/6/18 (Item 3 from file: 5)
08986935 BIOSIS NO.: 199396138436
Progenitor cell hyperplasia with rare development of myeloid leukemia in **interleukin** 11 bone marrow chimeras.
1993

4/6/19 (Item 4 from file: 5)
08832233 BIOSIS NO.: 199395121584
Human **stem** cell factor (c-kit ligand) induces an autocrine **loop**

of growth in a GM-CSF-depend megakaryocytic leukemia cell [redacted].
1993

4/6/20 (Item 5 from file: 5)
05203177 BIOSIS NO.: 000082043799
IDENTIFICATION OF A POSITIVE RETROREGULATOR THAT STABILIZES MESSENGER **RNA** SPECIES IN BACTERIA
1986

4/6/21 (Item 1 from file: 357)
0047839 DBA Accession No.: 86-05687
New positive retroregulatory element - useful for ligation downstream of DNA sequence expressionable for gene product to enhance expression
1996

4/6/22 (Item 1 from file: 73)
11285555 EMBASE No: 2001295261
Double-stranded RNA regulates IL-4 expression
01 SEP 2001

4/6/23 (Item 2 from file: 73)
10751725 EMBASE No: 2000231911
Translational pathophysiology: A novel molecular mechanism of human disease
01 JUN 2000

4/6/24 (Item 3 from file: 73)
06389337 EMBASE No: 1996038191
Regulation of murine macrophage IL-12 production: Activation of macrophages in vivo, restimulation in vitro, and modulation by other cytokines
1996

4/6/25 (Item 4 from file: 73)
06040056 EMBASE No: 1995070323
Cell-to-cell interaction of cytokine-dependent myeloblastic line constitutively expressing membrane-bound **stem** cell factor abrogates cytokine dependency partially through granulocyte-macrophage colony-stimulating factor production
1995

4/6/26 (Item 5 from file: 73)
05481966 EMBASE No: 1993250065
The SCL gene product is regulated by and differentially regulates cytokine responses during myeloid leukemic cell differentiation
1993

4/6/27 (Item 6 from file: 73)
04901544 EMBASE No: 1992041759
Ferritin gene expression in health and malignancy
1992
? s loop and (double (w) stranded)

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          121850  LOOP
          520065  DOUBLE
           92974  STRANDED
           45698  DOUBLE(W)STRANDED
      S5    1243  LOOP AND (DOUBLE (W) STRANDED)
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? s s5 and RNA

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          1243  S5
        900435  RNA
     S6     685  S5 AND RNA
? s s6 and interleukin

           685  S6
        348829  INTERLEUKIN
     S7       2  S6 AND INTERLEUKIN
? rd

...completed examining records
     S8       2  RD (unique items)
? t s8/6/1-2


 8/6/1     (Item 1 from file: 73)
11285555     EMBASE No: 2001295261
  Double-stranded RNA regulates IL-4 expression
  01 SEP 2001


 8/6/2     (Item 2 from file: 73)
06389337     EMBASE No: 1996038191
  Regulation of murine macrophage IL-12 production: Activation of
macrophages in vivo, restimulation in vitro, and modulation by other
cytokines
  1996
? t s8/7/1-2


 8/7/1     (Item 1 from file: 73)
DIALOG(R)File  73:EMBASE
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11285555     EMBASE No: 2001295261
  Double-stranded RNA regulates IL-4 expression
  Kehoe K.E.; Brown M.A.; Imani F.
  Dr. F. Imani, Division of Clinical Immunology, Department of Medicine,
  Johns Hopkins Univ. Sch. of Medicine, 5501 Hopkins Bayview Circle,
  Baltimore, MD 21224  United States
  AUTHOR EMAIL: fimani@mail.jhmi.edu
  Journal of Immunology ( J. IMMUNOL. ) (United States)   01 SEP 2001,
  167/5 (2496-2501)
  CODEN: JOIMA   ISSN: 0022-1767
  DOCUMENT TYPE: Journal ; Article
  LANGUAGE: ENGLISH   SUMMARY LANGUAGE: ENGLISH
  NUMBER OF REFERENCES: 39

  dsRNA, as genomic fragment, replicative intermediate, or stem and
loop structure in cells infected by viruses, can act to signal the
immune system of the presence of viral infections. Although most viral
infections are associated with strong Th1 immune responses, Th2-type
responses have also been observed. In this study, we characterize the
effects of dsRNA on the induction of Th2 responses in human lymphocytes. We
report that in addition to the well-known Th1-inducing capabilities of
dsRNA, treatment of human lymphocytes with low concentrations of dsRNA
(0.1-1 mug/ml) leads to the expression of the prototypic Th2 cytokine IL-4.
This induction was accompanied with the concentration-dependent activation
of NF-kappaB and NF-AT2 but not NF-AT1. In addition, dsRNA can directly
activate an IL-4 promoter-driven chloramphenicol acetyltransferase reporter
gene in transiently transfected Jurkat cells. These results are the first
demonstration of a non-TCR-associated activator of NF-AT in human cells and
suggest that dsRNA directly influences IL-4 gene expression through its
effect on NF-AT activation. Our data provide support for the idea that
dsRNA at low concentrations in vivo may induce a Th2-dominant response that
is not optimal for protective immunity to the virus.
```

8/7/2 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

06389337 EMBASE No: 1996038191
Regulation of murine macrophage IL-12 production: Activation of macrophages in vivo, restimulation in vitro, and modulation by other cytokines
Skeen M.J.; Miller M.A.; Shinnick T.M.; Ziegler H.K.
Dept. of Microbiology and Immunology, Rollins Research Center, Emory University,Atlanta, GA 30322 United States
Journal of Immunology (J. IMMUNOL.) (United States) 1996, 156/3 (1196-1206)
CODEN: JOIMA ISSN: 0022-1767
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

IL-12 is important in the host response to a variety of pathogens. It plays an adjuvant-like role in an initial immune response as well as a therapeutic role in established infections. Despite its well documented importance, comparatively little is known about the regulation of IL-12 production. In this study, we examined IL-12 production by cultured murine peritoneal macrophages from two perspectives: 1) macrophage activation in vivo, and 2) stimulation of IL-12 secretion in vitro. Macrophages were maximally activated within 48 h in vivo during infection with Listeria. Interestingly, although avirulent or heat-killed Listeria induced only minimal production of IL-12 by macrophages, the immunogenic combination of heat-killed bacteria and rIL-12 was highly stimulatory for IL-12 production. LPS and peritoneal inflammatory agents were also stimulatory, but latex heads were ineffective, indicating that microbial components were essential and phagocytosis alone was insufficient. Restimulation in vitro revealed similar patterns, in that infection and LPS were stimulatory but latex beads were not. A systematic survey of potential stimulatory agents showed that microbial heat shock proteins, crude bacterial extracts, bacterial superantigens, a yeast extract, and dsRNA induced IL-12 in vitro. Other cytokines also influenced IL-12 induction. IFN-gamma, which is up-regulated during infection, acted in synergy with other stimuli, suggesting an amplification **loop** for IL-12 production, whereas IL-4, IL-10, IL-13, and TGF- beta were inhibitory. The existence of a broad range of stimuli from a wide variety of pathogenic organisms underscores the fundamental importance of IL- 12 in host defense.
? ds

Set	Items	Description
S1	10500	LOOP AND ((DOUBLE (W) STRANDED) OR STEM)
S2	7314	S1 AND RNA
S3	38	S2 AND INTERLEUKIN
S4	27	RD (unique items)
S5	1243	LOOP AND (DOUBLE (W) STRANDED)
S6	685	S5 AND RNA
S7	2	S6 AND INTERLEUKIN
S8	2	RD (unique items)

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? s s5 and interleukin

          1243  S5
        348829  INTERLEUKIN
     S9       6  S5 AND INTERLEUKIN
? rd

...completed examining records
    S10       4  RD (unique items)
? t s10/6/1-4
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10/6/1 (Item 1 from file: [redacted])
09197808 97136883 PMID: 8982260
Peptide nucleic acids directed to the promoter of the alpha-chain of the **interleukin**-2 receptor.
Dec 11 1996

10/6/2 (Item 1 from file: 357)
0016754 DBA Accession No.: 84-00029
Cloning of **double stranded** cDNA from major and minor components of mRNA - role of reverse-transcriptase review e.g. Pseudopleuronectus americanus antifreeze and T leukocyte **interleukin** 2 cDNA cloning (conference paper) 1982

10/6/3 (Item 1 from file: 73)
11285555 EMBASE No: 2001295261
Double-stranded RNA regulates IL-4 expression
01 SEP 2001

10/6/4 (Item 2 from file: 73)
06389337 EMBASE No: 1996038191
Regulation of murine macrophage IL-12 production: Activation of macrophages in vivo, restimulation in vitro, and modulation by other cytokines
1996
? t s10/7/1-4

10/7/1 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09197808 97136883 PMID: 8982260
Peptide nucleic acids directed to the promoter of the alpha-chain of the **interleukin**-2 receptor.
Praseuth D; Grigoriev M; Guieysse AL; Pritchard LL; Harel-Bellan A; Nielsen PE; Helene C
Laboratoire de Biophysique, INSERM U.201-CNRS URA 481, Museum National d'Histoire Naturelle, Paris, France. praseuth@mnhn.fr
Biochimica et biophysica acta (NETHERLANDS) Dec 11 1996, 1309 (3) p226-38, ISSN 0006-3002 Journal Code: A0W
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
Two 10-mer oligopyrimidine peptide nucleic acids (PNAs) were designed to interfere with IL-2R alpha promoter expression by binding to the regulatory sequences overlapping SRF and NF-kappa B transcription factor sites. Specific complexes were formed on each target sequence, and clearly involved (1) Hoogsteen hydrogen bonds as shown by experiments in which the purine strand of a single or **double-stranded** target was substituted with 7-deazadeoxyguanosine, (2) P-**loop** formation on double-helical DNA as evidenced by susceptibility to a single-strand-specific nuclease. When formed on a single-stranded DNA target, these highly stable complexes were responsible for efficient physical blockage of T7 DNA polymerase elongation on the template DNA containing the target oligopurine sequence. On a **double-stranded** target, these complexes only formed at low ionic strength and were slowly dissociated at physiological ionic strength (pH 6.5) with a t1/2 of 6.5-7 h. The salt-dependent instability of preformed complexes on a plasmid target was probably the critical factor responsible for their lack of significant sequence-specific effect on IL-2R alpha promoter activity inside living cells.
Record Date Created: 19970122

10/7/2 (Item 1 from file: 357)

DIALOG(R)File 357:Derwent Biot[redacted]nology Abs
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0016754 DBA Accession No.: 84-00029
Cloning of **double stranded** cDNA from major and minor components of mRNA - role of reverse-transcriptase review e.g. Pseudopleuronectus americanus antifreeze and T leukocyte **interleukin** 2 cDNA cloning (conference paper)
AUTHOR: Lin Y
CORPORATE SOURCE: Biological Carcinogenesis Program, National Cancer Institute-Frederick Cancer Research Facility, Frederick, Maryland, USA.
(111-27) 1982
CODEN: 9999Z
LANGUAGE: English
ABSTRACT: Mature mRNA specific for certain proteins is found in the cytoplasm where it actively synthesizes these proteins. Methods of isolating and purifying poly(A)-mRNA are briefly discussed. In the synthesis of single-stranded (ss)-DNA from mRNA, reverse-transcriptase is used for ss-DNA synthesis; mRNA is dissociated from the cDNA-mRNA complex and the enzyme is denatured by boiling; the mixture is centrifuged ; DNA polymerase I is added to the supernatant for the synthesis of **double-stranded** (ds)-DNA. The hair-pin **loop** appearing by chance on the ss-cDNA and serving as primer for ds-DNA synthesis, is removed to give an open-ended ds-cDNA used for insertion into a plasmid. The hybrid plasmid can then be used to transform a host organism such as Escherichia coli. The application of these techniques in the cloning of antifreeze cDNA from Pseudopleuronectus americanus and **interleukin** 2 cDNA from monkey T leukocytes is described. New cloning vectors and cloning procedures are discussed. (41 ref)

10/7/3 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE
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11285555 EMBASE No: 2001295261
Double-stranded RNA regulates IL-4 expression
Kehoe K.E.; Brown M.A.; Imani F.
Dr. F. Imani, Division of Clinical Immunology, Department of Medicine, Johns Hopkins Univ. Sch. of Medicine, 5501 Hopkins Bayview Circle, Baltimore, MD 21224 United States
AUTHOR EMAIL: fimani@mail.jhmi.edu
Journal of Immunology (J. IMMUNOL.) (United States) 01 SEP 2001, 167/5 (2496-2501)
CODEN: JOIMA ISSN: 0022-1767
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 39

dsRNA, as genomic fragment, replicative intermediate, or stem and **loop** structure in cells infected by viruses, can act to signal the immune system of the presence of viral infections. Although most viral infections are associated with strong Th1 immune responses, Th2-type responses have also been observed. In this study, we characterize the effects of dsRNA on the induction of Th2 responses in human lymphocytes. We report that in addition to the well-known Th1-inducing capabilities of dsRNA, treatment of human lymphocytes with low concentrations of dsRNA (0.1-1 mug/ml) leads to the expression of the prototypic Th2 cytokine IL-4. This induction was accompanied with the concentration-dependent activation of NF-kappaB and NF-AT2 but not NF-AT1. In addition, dsRNA can directly activate an IL-4 promoter-driven chloramphenicol acetyltransferase reporter gene in transiently transfected Jurkat cells. These results are the first demonstration of a non-TCR-associated activator of NF-AT in human cells and suggest that dsRNA directly influences IL-4 gene expression through its effect on NF-AT activation. Our data provide support for the idea that dsRNA at low concentrations in vivo may induce a Th2-dominant response that

is not optimal for protective i[redacted]nity to the virus.

10/7/4 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

06389337 EMBASE No: 1996038191
Regulation of murine macrophage IL-12 production: Activation of macrophages in vivo, restimulation in vitro, and modulation by other cytokines
Skeen M.J.; Miller M.A.; Shinnick T.M.; Ziegler H.K.
Dept. of Microbiology and Immunology, Rollins Research Center, Emory University,Atlanta, GA 30322 United States
Journal of Immunology (J. IMMUNOL.) (United States) 1996, 156/3 (1196-1206)
CODEN: JOIMA ISSN: 0022-1767
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

IL-12 is important in the host response to a variety of pathogens. It plays an adjuvant-like role in an initial immune response as well as a therapeutic role in established infections. Despite its well documented importance, comparatively little is known about the regulation of IL-12 production. In this study, we examined IL-12 production by cultured murine peritoneal macrophages from two perspectives: 1) macrophage activation in vivo, and 2) stimulation of IL-12 secretion in vitro. Macrophages were maximally activated within 48 h in vivo during infection with Listeria. Interestingly, although avirulent or heat-killed Listeria induced only minimal production of IL-12 by macrophages, the immunogenic combination of heat-killed bacteria and rIL-12 was highly stimulatory for IL-12 production. LPS and peritoneal inflammatory agents were also stimulatory, but latex heads were ineffective, indicating that microbial components were essential and phagocytosis alone was insufficient. Restimulation in vitro revealed similar patterns, in that infection and LPS were stimulatory but latex beads were not. A systematic survey of potential stimulatory agents showed that microbial heat shock proteins, crude bacterial extracts, bacterial superantigens, a yeast extract, and dsRNA induced IL-12 in vitro. Other cytokines also influenced IL-12 induction. IFN-gamma, which is up-regulated during infection, acted in synergy with other stimuli, suggesting an amplification **loop** for IL-12 production, whereas IL-4, IL-10, IL-13, and TGF- beta were inhibitory. The existence of a broad range of stimuli from a wide variety of pathogenic organisms underscores the fundamental importance of IL- 12 in host defense.
? ds

Set	Items	Description
S1	10500	LOOP AND ((DOUBLE (W) STRANDED) OR STEM)
S2	7314	S1 AND RNA
S3	38	S2 AND INTERLEUKIN
S4	27	RD (unique items)
S5	1243	LOOP AND (DOUBLE (W) STRANDED)
S6	685	S5 AND RNA
S7	2	S6 AND INTERLEUKIN
S8	2	RD (unique items)
S9	6	S5 AND INTERLEUKIN
S10	4	RD (unique items)

? t s4/7/4-8, 10-12, 21, 23, 27

4/7/4 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09281337 97223466 PMID: 9070287
A minimised hammerhead ribozyme with activity against **interleukin**-2 in human cells.

Sioud M; Opstad A; Hendry P; [redacted]ckett TJ; Jennings PA; McCall [redacted]
Institute of Immunology and Rheumatology, National Hospital, Oslo, Norway.
Biochemical and biophysical research communications (UNITED STATES) Feb 13 1997, 231 (2) p397-402, ISSN 0006-291X Journal Code: 9Y8
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
A "minizyme" is a smaller version of the hammerhead ribozyme, in which **stem-loop** II has been replaced by a short linker. Here, we have synthesised a DNA-containing minizyme and a ribozyme, which are designed to cut within a 15-nucleotide sequence in human **interleukin**-2 mRNA, and have tested for their activity in vitro and in cells. In vitro at 37 degrees C, a minizyme with linker of sequence d(GTTTT) cleaves a 15-ribonucleotide synthetic substrate 5-fold slower than does the full-sized ribozyme. In human cells, the minizyme inhibits the production of **interleukin** -2 protein to a similar extent as does the ribozyme. Also, the minizyme and the ribozyme are more effective in cells than any of three controls: an inactive minizyme, a 15-nucleotide antisense DNA, or DNA of random sequence. The positive effect observed in cells indicates that minizymes may be useful as pharmaceuticals.
Record Date Created: 19970417

4/7/5 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09269258 97211760 PMID: 9058727
CD30 ligand is frequently expressed in human hematopoietic malignancies of myeloid and lymphoid origin.
Gattei V; Degan M; Gloghini A; De Iuliis A; Improta S; Rossi FM; Aldinucci D; Perin V; Serraino D; Babare R; Zagonel V; Gruss HJ; Carbone A; Pinto A
Department of Medical Oncology, Centro di Riferimento Oncologico, INRCCS, Aviano, Italy.
Blood (UNITED STATES) Mar 15 1997, 89 (6) p2048-59, ISSN 0006-4971 Journal Code: A8G
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
CD30 ligand (CD30L) is a type-II membrane glycoprotein capable of transducing signals leading to either cell death or proliferation through its specific counterstructure CD30. Although several lines of evidence indicate that CD30L plays a key role as a paracrine- or autocrine-acting surface molecule in the deregulated cytokine cascade of Hodgkin's disease, little is known regarding its distribution and biologic significance in other human hematopoietic malignancies. By analyzing tumor cells from 181 patients with **RNA** studies and immunostaining by the anti-CD30L monoclonal antibody M80, we were able to show that human hematopoietic malignancies of different lineage and maturation stage display a frequent and broad expression of the ligand. CD30L mRNA and surface protein were detected in 60% of acute myeloid leukemias (AMLs), 54% of B-lineage acute lymphoblastic leukemias (ALLs), and in a consistent fraction (68%) of B-cell lymphoproliferative disorders. In this latter group, hairy cell leukemia and high-grade B-cell non-Hodgkin's lymphoma (B-NHL) expressed a higher surface density of CD30L as compared with B-cell chronic lymphocytic leukemia and low-grade B-NHL. Purified plasmacells from a fraction of multiple myeloma patients also displayed CD30L mRNA and protein. A more restricted expression of CD30L was found in T-cell tumors that was mainly confined to neoplasms with an activated peripheral T-cell phenotype, such as T-cell prolymphocytic leukemia, peripheral T-NHL, and adult T-cell leukemia/lymphoma. In contrast, none of the T-lineage ALLs analyzed expressed the ligand. In AML, a high cellular density of CD30L was detected in French-American-British M3, M4, and M5 phenotypes, which are directly associated with the presence on tumor cells of certain surface structures, including the p55 **interleukin**-2 receptor alpha-chain, the alpha(M) (CD11b) chain of beta2 integrins, and the intercellular adhesion molecule-1

(CD54). Analysis of normal hematopoietic cells evidenced that, addition to circulating and tonsil B cells, a fraction of bone marrow myeloid precursors, erythroblasts, and subsets of megakaryocytes also express CD30L. Finally, we have shown that native CD30L expressed on primary leukemic cells is functionally active by triggering both mitogenic and antiproliferative signals on CD30+ target cells. As opposed to CD30L, only 10 of 181 primary tumors expressed CD30 mRNA or protein, rendering therefore unlikely a CD30-CD30L autocrine **loop** in human hematopoietic neoplasms. Taken together, our data indicate that CD30L is widely expressed from early to late stages of human hematopoiesis and suggest a regulatory role for this molecule in the interactions of normal and malignant hematopoietic cells with CD30+ immune effectors and/or microenvironmental accessory cells.

Record Date Created: 19970402

4/7/6 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09181168 96430277 PMID: 8833403

C-kit ligand (SCF) in human multiple myeloma cells.

Lemoli RM; Fortuna A
Institute of Hematology, University of Bologna, Italy.

Leukemia & lymphoma (SWITZERLAND) Feb 1996, 20 (5-6) p457-64, ISSN 1042-8194 Journal Code: BNQ
Languages: ENGLISH
Document type: Journal Article
Record type: Completed

Here we review our recent experience addressing the role of SCF in multiple myeloma (MM). We first investigated the proliferation of MM cell lines and bone marrow samples from myeloma patients in response to rh-SCF alone and combined with **Interleukin**-6 (IL-6), IL-3, and IL-3/GM-CSF fusion protein PIXY 321. Neoplastic plasma cells were highly purified (>90%) by immunomagnetic depletion of T, myeloid, monocytoid and NK cells. The number of S-phase cells was evaluated after 3 days of liquid culture by the bromodeoxyuridine (BRDU) incorporation assay. The proliferation of RPMI 8226 and U266 cell lines was also assessed by a clonogenic assay. All the experiments were performed in serum-free conditions. RPMI 8226 cell line was not stimulated by SCF which also did not augment the proliferative activity of IL-6, IL-3 and PIXY-321. Conversely, SCF addition resulted in 2.4-fold increase of the number of U266 colonies and in a higher number of U266 and MT3 cells in S-phase. The c-kit ligand also enhanced the proliferation of MT3 and U266 cells mediated by the other cytokines. Anti-SCF polyclonal antibodies completely abrogated the proliferative response of MT3 cells to exogenous SCF and markedly reduced the spontaneous growth of the same cell line. Reverse transcriptase-polymerase chain reaction amplification (RT-PCR) did detect SCF mRNA in MT3 and RPMI 8226 cells. Moreover, secreted SCF was found, in a biologically active form, in the supernatant of the two cell lines by the MO7e proliferation assay. These results suggest that an autocrine proliferative **loop** may be operative in MT3 cell line. When tested on fresh myeloma samples, SCF increased the number of S-phase plasma cells (4.7 +/- 1.6% vs 3.4 +/- 1.3% in control cultures; p = 0.02). Significant proliferation was also induced by IL6, IL-3 and PIXY-321. The addition of SCF significantly enhanced the proliferation of myeloma cells responsive to IL-6. Preliminary experiments performed on circulating plasma cells and myeloma precursors further supported the role of SCF on the proliferation of the neoplastic clone in MM.

Record Date Created: 19970612

4/7/7 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09172502 96354215 PMID: 8761952

Expression of basic helix-**loop** -helix transcription factors in explant hematopoietic progenitors.

Quesenberry PJ; Iscove NN[redacted]ooper C; Brady G; Newburger P tein GS; Stein JS; Reddy GP; Pearson-White S

Cancer Center, University of Massachusetts Medical Center, Worcester 01605, USA.

Journal of cellular biochemistry (UNITED STATES) Jun 1 1996, 61 (3) p478-88, ISSN 0730-2312 Journal Code: HNF

Contract/Grant No.: 5R01 CA27466-17, CA, NCI

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

The basic helix-**loop** -helix (bHLH) transcription factors form heterodimers and control steps in cellular differentiation. We have studied four bHLH transcription factors, SCL, lyl-1, E12/E47, and ld-1, in individual lineage-defined progenitors and hematopoietic growth factor-dependent cell lines, evaluating mRNA expression and the effects of growth factors and cell cycle phase on this expression. Single lineage-defined progenitors selected from early murine colony starts and grown under permissive conditions were analyzed by RT-PCR. SCL and E12/E47 were expressed in the vast majority of tri-, bi-, and unilineage progenitors of erythroid, macrophage, megakaryocyte, and neutrophil lineages. Expression for E12/E47 was not seen in unilineage megakaryocyte and erythroid or bilineage neutrophil/mast cell progenitors. Lyl-1 showed a more restricted pattern of expression, although expression was seen in some bi- and unilineage progenitors. No expression was detected in erythroid, erythroid-megakaryocyte-macrophage, macrophage-neutrophil, macrophage, or megakaryocytic progenitors. Id-1, an inhibitory bHLH transcription factor, was also widely expressed in all bi- and unilineage progenitors; only the trilineage erythroid-megakaryocyte-macrophage progenitors failed to show expression. Expression of these factors within a progenitor class was generally heterogeneous, with some progenitors showing expression and some not. This was seen even when two sister cells from the same colony start were analyzed. Id-1, but not E12/E47, mRNA was increased in FDC-P1 and MO7E hematopoietic cell lines after exposure to IL-3 or GM-CSF. Id-1, E12, and lyl-1 showed marked variation at different points in cell cycle in isoleucine-synchronized FDC-P1 cells. These results suggest that SCL, lyl-1, E12/E47, and Id-1 are important in hematopoietic progenitor cell regulation, and that their expression in hematopoietic cells varies in response to cytokines and/or during transit through cell cycle.

Record Date Created: 19970429

4/7/8 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09088756 97098461 PMID: 8943001

A cytokine mRNA-destabilizing element that is structurally and functionally distinct from A+U-rich elements.

Brown CY; Lagnado CA; Goodall GJ

Hanson Centre for Cancer Research, Institute of Medical and Veterinary Science, Adelaide, Australia.

Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Nov 26 1996, 93 (24) p13721-5, ISSN 0027-8424 Journal Code: PV3

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

The control of mRNA stability is crucial to the regulation of cytokine expression. We describe here a novel, potent destabilizing element found in the 3' untranslated region of granulocyte colony-stimulating factor mRNA. This element, which appears to require at least one **stem-loop** structure, we term the **stem-loop** destabilizing element (SLDE). Functionally equivalent elements appear to also exist in the **interleukin** 2 and **interleukin** 6 mRNAs. The SLDE is functionally distinct from the A+U-rich elements, which are also present in these and other cytokine mRNAs, because it destabilizes a chimeric mRNA in a tumor cell line in which A+U-rich elements do not function. In addition, the effect of the SLDE is insensitive to calcium ionophore and is therefore

regulated independently of A+U [redacted]stabilizing elements. The exis[redacted]ce of two distinct mRNA-destabilizing elements provides an additional mechanism for the differential regulation of cytokine expression.
Record Date Created: 19970116

4/7/10 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08866964 96184798 PMID: 8605355
Plasma cells induce apoptosis of pre-B cells by interacting with bone marrow stromal cells.
Tsujimoto T; Lisukov IA; Huang N; Mahmoud MS; Kawano MM
Department of Hematology and Oncology, Research Institute for Radiation Biology and Medicine, Hiroshima University, Japan.
Blood (UNITED STATES) Apr 15 1996, 87 (8) p3375-83, ISSN 0006-4971 Journal Code: A8G
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
By using two-color phenotypic analysis with fluorescein isothiocyanate-anti-CD38 and phycoerythrin-anti-CD19 antibodies, we found that pre-B cells (CD38+CD19+) signifcantly decreased depending on the number of plasma cells (CD38++CD19+) in the bone marrow (BM) in the cases with BM plasmacytosis, such as myelomas and even polyclonal gammopathy. To clarify how plasma cells suppress survival of pre-B cells, we examined the effect of plasma cells on the survival of pre-B cells with or without BM-derived stromal cells in vitro. Pre-B cells alone rapidly entered apoptosis, but **interleukin**-7 (IL-7), a BM stromal cell line (KM-102), or culture supernatants of KM-102 cells could support pre-B cell survival. On the other hand, inhibitory factors such as transforming growth factor-beta1 (TGF-beta1) and macrophage inflammatory protein-1beta (MIP-1beta) could suppress survival of pre-B cells even in the presence of IL-7. Plasma cells alone could not suppress survival of pre-B cells in the presence of IL-7, but coculture of plasma cells with KM-102 cells or primary BM stromal cells induced apoptosis of pre-B cells. Supernatants of coculture with KM-102 and myeloma cell lines (KMS-5) also could suppress survival of pre-B cells. Furthermore, we examined the expression of IL-7, TGF-beta1, and MIP-1beta mRNA in KM-102 cells and primary stromal cells cocultured with myeloma cell lines (KMS-5). In these cells, IL-7 mRNA was downregulated, but the expression of TGF-beta1 and MIP-1beta mRNA was augmented. Therefore, these results suggest that BM-derived stromal cells attached to plasma (myeloma) cells were modulated to secrete lesser levels of supporting factor (IL-7) and higher levels of inhibitory factors (TGF-beta1 and MIP-1beta) for pre-B cell survival, which could explain why the increased number of plasma (myeloma) cells induced suppression of pre-B cells in the BM. This phenomenon may represent a feedback **loop** between pre-B cells and plasma cells via BM stromal cells in the BM.
Record Date Created: 19960517

4/7/11 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08425692 94229206 PMID: 7513651
A murine stromal cell line promotes the proliferation of the human factor-dependent leukemic cell line UT-7.
Auffray I; Dubart A; Izac B; Vainchenker W; Coulombel L
INSERM U 362, Institut Gustave Roussy, Villejuif, France.
Experimental hematology (UNITED STATES) May 1994, 22 (5) p417-24, ISSN 0301-472X Journal Code: EPR
Languages: ENGLISH
Document type: Journal Article
Record type: Completed
In long-term human bone marrow cultures, stromal cells of human origin are usually used on the assumption that human primitive progenitor cells do not respond to cytokines produced by stromal cells from other species.

There is accumulating evide[redacted] however, that murine stroma[redacted]ells also promote maintenance and differentiation of very primitive human **stem** cells, which suggests the existence of novel stromal activities that cross species barriers. In this study, we show that a murine bone marrow-derived stromal cell line, MS-5, allows the proliferation of the human leukemic cell line UT-7. The long-term growth of UT-7 is usually supported only by human **interleukin**-3 (IL-3), granulocyte-macrophage colony-stimulating factor (GM-CSF), or erythropoietin (Epo). None of these three cytokines was involved in the observed effect, since murine GM-CSF and IL-3 do not act on human cells and MS-5 cells do not produce Epo. Soluble **stem** cell factor (SCF) induced UT-7 cell proliferation. However, S1/S1 mutant fibroblasts also supported UT-7 cell growth and anti-c-kit antibodies only partially abolished UT-7 cell proliferative response to MS-5 cells. These observations excluded a major role of SCF in this system. MS-5-derived growth-promoting activity was diffusible, but attempts to grow UT-7 cells in high levels of known soluble murine stromal-derived cytokines active on human cells showed no or minimal response, suggesting that MS-5's proliferative effect was not mediated by known cytokines. Finally, involvement of an autocrine **loop** of activation induced by MS-5 was excluded: RT-PCR analysis did not detect increased transcripts for GM-CSF, IL-3, IL-6, SCF, or Epo in UT-7 cells cocultured for 2 to 6 days with MS-5. In addition, UT-7 cell proliferation on MS-5 was not inhibited by neutralizing antibodies against the human GM-CSF receptor or the human IL-6 receptor alpha chain. Whether UT-7 cell proliferation triggered by MS-5 reflects the existence of novel stromal cytokines or results from synergistic interactions on the MS-5 cell surface between extracellular matrix proteins and cytokines will require further investigation.

Record Date Created: 19940603

4/7/12 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08182737 94286556 PMID: 8016095

The E2A and tal-1 helix-**loop**-helix proteins associate in vivo and are modulated by Id proteins during **interleukin** 6-induced myeloid differentiation.

Voronova AF; Lee F

DNAX Research Institute of Molecular and Cellular Biology, Palo Alto, CA 94304-1104.

Proceedings of the National Academy of Sciences of the United States of America (UNITED STATES) Jun 21 1994, 91 (13) p5952-6, ISSN 0027-8424 Journal Code: PV3

Languages: ENGLISH

Document type: Journal Article

Record type: Completed

The immunoglobulin enhancer-binding proteins, E12 and E47, encoded by the E2A gene belong to the basic helix-**loop** -helix (bHLH) family of regulatory proteins and act as transcriptional activators. In addition to their critical role in B-lymphocyte development, the E12 and E47 proteins have been implicated in the induction of myogenesis as heterodimeric partners of myogenic bHLH proteins, MyoD and myogenin. Here we demonstrate that the E2A proteins form heterodimers with the bHLH oncoprotein tal-1 in myeloid and erythroid cells and that these heterodimers specifically bind to the CANNTG DNA motif. Heterodimerization with tal-1 represses transactivation by E47 and could function to prevent the expression of immunoglobulin genes in cells other than B lymphocytes. DNA binding by E2A-tal-1 heterodimers in the M1 mouse myeloid cell line is abrogated upon terminal macrophage differentiation induced by the cytokine **interleukin** 6. The loss of E2A-tal-1 DNA binding is correlated with elevated expression of mRNA encoding the dominant negative HLH proteins, Id1 and particularly Id2. Moreover, recombinant Id proteins inhibit the E2A-tal-1-specific DNA binding activity from undifferentiated M1 cells. These results suggest that E2A-tal-1 heterodimers may play a role in preventing terminal differentiation in the myeloid lineage and provide a possible explanation for oncogenic transformation induced by ectopic tal-1 expression in acute T-cell lymphoblastic leukemias.

Record Date Created: 1994072

4/7/21 (Item 1 from file: 357)
DIALOG(R)File 357:Derwent Biotechnology Abs

0047839 DBA Accession No.: 86-05687 PATENT
New positive retroregulatory element - useful for ligation downstream of DNA sequence expressionable for gene product to enhance expression
PATENT ASSIGNEE: Cetus 1996
PATENT NUMBER: EP 174785 PATENT DATE: 960319 WPI ACCESSION NO.: 86-077173 (8612)
PRIORITY APPLIC. NO.: US 717331 APPLIC. DATE: 850329
NATIONAL APPLIC. NO.: EP 85306183 APPLIC. DATE: 850830
LANGUAGE: English
ABSTRACT: A positive retroregulatory element which, when ligated downstream of a DNA sequence expressionable for a gene product (I), enhances the expression of (I) is new. Also new is a plasmid comprising a DNA sequence expressionable for a gene product (II) and a positive retroregulatory element ligated to the DNA sequence in a relationship to it, so that expression of (II) is enhanced. Cells transformed by the plasmid, and **RNA** sequences having an extended half-life conferred by a co-transcribed positive retroregulatory sequence are also new. The element preferably comprises the 3'-flanking sequence of Bacillus thuringiensis crystal protein gene containing an inverted repeat sequence. The **RNA** transcript of the inverted repeat sequence forms a **stem** and **loop** structure with a delta-G of -30.4 kcal/mole. Expression of (I) coded for by the DNA sequence is significantly increased with the positive retroregulatory element. (I) And (II) are especially beta-lactamase (EC-3.5.2.6) or mammal **interleukin** -2, and are expressed e.g. in Escherichia coli or Bacillus subtilis. (65pp)

4/7/23 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

10751725 EMBASE No: 2000231911
Translational pathophysiology: A novel molecular mechanism of human disease
Cazzola M.; Skoda R.C.
M. Cazzola, Division of Hematology, IRCCS Policlinico S. Matteo, 27100 Pavia Italy
AUTHOR EMAIL: m.cazzola@iol.it
Blood (BLOOD) (United States) 01 JUN 2000, 95/11 (3280-3288)
CODEN: BLOOA ISSN: 0006-4971
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 109

In higher eukaryotes, the expression of about 1 gene in 10 is strongly regulated at the level of messenger **RNA** (mRNA) translation into protein. Negative regulatory effects are often mediated by the 5'-untranslated region (5'-UTR) and rely on the fact that the 40S ribosomal subunit first binds to the cap structure at the 5'-end of mRNA and then scans for the first AUG codon. Self-complementary sequences can form stable **stem-loop** structures that interfere with the assembly of the preinitiation complex and/or ribosomal scanning. These **stem** loops can be further stabilized by the interaction with **RNA**-binding proteins, as in the case of ferritin. The presence of AUG codons located upstream of the physiological start site can inhibit translation by causing premature initiation and thereby preventing the ribosome from reaching the physiological start codon, as in the case of thrombopoietin (TPO). Recently, mutations that cause disease through increased or decreased efficiency of mRNA translation have been discovered, defining translational

pathophysiology as a novel mechanism of human disease. Hereditary hyperferritinemia/cataract syndrome arises from various point mutations or deletions within a protein-binding sequence in the 5'-UTR of the L-ferritin mRNA. Each unique mutation confers a characteristic degree of hyperferritinemia and severity of cataract in affected individuals. Hereditary thrombocythemia (sometimes called familial essential thrombocythemia or familial thrombocytosis) can be caused by mutations in upstream AUG codons in the 5'-UTR of the TPO mRNA that normally function as translational repressors. Their inactivation leads to excessive production of TPO and elevated platelet counts. Finally, predisposition to melanoma may originate from mutations that create translational repressors in the 5'-UTR of the cyclin-dependent kinase inhibitor-2A gene.

4/7/27 (Item 6 from file: 73)
DIALOG(R)File 73:EMBASE

04901544 EMBASE No: 1992041759
Ferritin gene expression in health and malignancy
Bomford A.B.; Munro H.N.
USDA Human Nutrition Research, 711 Washington Street,Boston, MA 02111
United States
Pathobiology (PATHOBIOLOGY) (Switzerland) 1992, 60/1 (10-18)
CODEN: PATHE ISSN: 1015-2008
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Intracellular iron can be stored in the protein shell of ferritin to protect the cell against the toxic action of the iron. In response to increased cell iron, more ferritin subunits are synthesized using translational and transcriptional mechanisms. Translational control involves a unique **stem-loop** structure in the 5' untranslated region of the subunit messengers. When iron level is low, a protein binds to this **stem-loop** structure and prevents translation. When intracellular iron level rises, the repressor protein is discharged and the large population of messengers begins to translate subunits. Similar **stem-loop** motifs occur in the 3' untranslated region of the transferrin receptor messenger where they regulate breakdown of the receptor mRNA. Finally, the presence of excess iron preferentially stimulates transcription of more ferritin message of one type (L-mRNA) which produces ferritin shells favoring iron storage. In this way, protection of the cell against iron excess is enhanced by coordinate changes in rate of synthesis of ferritin mRNA of the L-type, by release of ferritin mRNA stored in the cytoplasm, and by a reduction in the number of receptors for accepting iron into the cell. The application of these principles with reference to malignant cells is discussed.
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S3	38	S2 AND INTERLEUKIN
S4	27	RD (unique items)
S5	1243	LOOP AND (DOUBLE (W) STRANDED)
S6	685	S5 AND RNA
S7	2	S6 AND INTERLEUKIN
S8	2	RD (unique items)
S9	6	S5 AND INTERLEUKIN
S10	4	RD (unique items)

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E6        23  AU=ECKER A.
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E9         3  AU=ECKER AD
E10        1  AU=ECKER ALFRED
E11        4  AU=ECKER AXEL
E12       14  AU=ECKER B

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E14        2  AU=ECKER BERNHARD
E15        1  AU=ECKER BP
E16        1  AU=ECKER BRUCE
E17       19  AU=ECKER C
E18        3  AU=ECKER C P
E19        6  AU=ECKER C.
E20        4  AU=ECKER C.P.
E21        1  AU=ECKER CH.
E22        1  AU=ECKER CHRISTA
E23        3  AU=ECKER CHRISTIAN
E24        2  AU=ECKER CP

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E27       95  AU=ECKER D J
E28        1  AU=ECKER D J J
E29        7  AU=ECKER D M
E30        8  AU=ECKER D.
E31       54  AU=ECKER D.J.
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E33        1  AU=ECKER DANIEL
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E35       34  AU=ECKER DAVID J
E36        2  AU=ECKER DAWN

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              95  AU=ECKER D J
               0  E28OR E30
              54  AU=ECKER D.J.
               1  AU=ECKER DAVID
              34  AU=ECKER DAVID J
     S11     195  AU="ECKER D" OR AU="ECKER D J" OR E28OR E30 OR AU="ECKER
                  D.J." OR AU="ECKER DAVID" OR AU="ECKER DAVID J"
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...examined 50 records  (150)
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S3         38   S2 AND INTERLEUKIN
S4         27   RD (unique items)
S5       1243   LOOP AND (DOUBLE (W) STRANDED)
S6        685   S5 AND RNA
S7          2   S6 AND INTERLEUKIN
S8          2   RD (unique items)
S9          6   S5 AND INTERLEUKIN
S10         4   RD (unique items)
S11       195   AU="ECKER D" OR AU="ECKER D J" OR E28OR E30 OR AU="ECKER D-
                .J." OR AU="ECKER DAVID" OR AU="ECKER DAVID J"
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 14/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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08768848   BIOSIS NO.: 199395058199
Implication of RNA structure on antisense oligonucleotide hybridization
  kinetics.
AUTHOR: Lima Walt F; Lonia Brett P; Ecker David J; Freier Susan M(a
AUTHOR ADDRESS: (a)Dep. Molecular, Cellular Biology, Isis Pharmaceuticals,
  2280 Faraday Avenue, Carlsbad, Calif. 92
JOURNAL: Biochemistry  31 (48):p12055-12061 1992
ISSN: 0006-2960
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: A 47-nucleotide transcript of the activated Ha-ras gene was
  prepared and determined, by enzymatic structure mapping, to form a stable
  hairpin structure. Six antisense decaribonucleotides were designed, and
  association constants (K-a) for the hairpin- and length-matched
  complements were measured. Two of the antisense oligonucleotides targeted
  to the loop had nearly equal affinity for the transcript compared
  to the complement. The others, including one oligonucleotide
  complementary to the 3' side of the single-stranded loop, bound
  10-5-10-6-fold less tightly to the transcript than to the short
  complement. We propose the difference in affinity is due to the target
  structure, both the secondary structure of the stem and the
  structure in the loop. Measurement of the bimolecular association
  rate constant, k-1, and the dissociation rate constant, k-1, for these
  oligonucleotides indicates the observed relationship between affinity and
  structure is primarily due to k-1.


 14/7/2     (Item 2 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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08376901 BIOSIS NO.: 000094[illegible]05
ENHANCEMENT OF RIBOSOMAL FRAMESHIFTING BY OLIGONUCLEOTIDES TARGETED TO THE HIV GAG-POL REGION
AUTHOR: VICKERS T A; **ECKER D J**
AUTHOR ADDRESS: ISIS PHARM., 2280 FARADAY AVE., CARLSBAD, CALIF. 92008.
JOURNAL: NUCLEIC ACIDS RES 20 (15). 1992. 3945-3953. 1992
FULL JOURNAL NAME: Nucleic Acids Research
CODEN: NARHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The pol gene of all retroviruses is expressed as a gag-pol fusion protein which is proteolytically processed to produce all viral enzymes. In the human immunodeficiency virus (HIV), the gag and pol genes overlap by 241 nucleotides with pol in the -1 phase with respect to gag. The gag-pol fusion is produced via a -1 ribosomal frameshifting event that brings the overlapping, out-of-phase gag and pol genes into translational phase. Frameshifting occurs at a so called 'shift site' 8-10 nucleotides upstream of a hairpin **loop** which may play a role in the regulation of frameshifting. We have fused this region of HIV-1 to the 5' end of the firefly luciferase reporter gene in order to quantitatively measure ribosomal frameshifting both in cells and by in vitro translation. A series of 2'-O-methyl oligonucleotides was designed to specifically bind the sequences which flank the gag-pol hairpin. Ribosomal frameshifting is enhanced up to 6 fold by those oligonucleotides which bind the area just 3 to the **stem**. Oligonucleotides which binds 5' to the **stem** have no effect on frameshift efficiency. In addition, we have constructed a series of fusion genes which mimic the effect of the bound oligonucleotides with intramolecular hairpins. The results suggest that increasing RNA secondary structure downstream of the shift site increases the frequency of ribosomal frameshifting, and that this effect can be mimicked by antisense oligonucleotides.

14/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07750102 BIOSIS NO.: 000092063823
INHIBITION OF HIV-LTR GENE EXPRESSION BY OLIGONUCLEOTIDES TARGETED TO THE TAR ELEMENT
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ABSTRACT: All human immunodeficiency virus mRNAs contain a sequence known as TAR (trans-activating responsive sequence). The TAR element forms a stable RNA **stem-loop** structure which binds the HIV tat (trans-activator) protein and mediates increased viral gene expression. In principle, molecules which bind to the TAR RNA structure would inhibit trans-activation by perturbing the native RNA secondary structure. We have constructed a series of phosphodiester and phosphorothioate antisense oligonucleotides which specifically bind to the HIV TAR element. Specific binding to the TAR element was demonstrated in vitro with enzymatically synthesized TAR RNA. The TAR-directed phosphorothioates inhibited trans-activation in a sequence-dependent fashion in a cell culture model using an HIV LTR/human placental alkaline phosphatase gene fusion and tat protein supplied in trans. The molecules also inhibited HIV replication in both acute and chronically infected viral assays, but without sequence specificity. We have constructed a series of vectors consisting of the MMTV promoter and 5'-untranslated region of four different mRNAs, including the TAR region, to study the

effect of TAR on gene expression in heterologous systems. The results suggest that, in the absence of the HIV LTR, the TAR element has a repressive effect on gene expression, which is relieved by tat.

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0236099 DBA Accession No.: 99-06200 PATENT
New oligonucleotides for modulating gene expression by RNA mimicry - RNA probe for use in disease diagnosis and RNA oligonucleotide for use in HIV virus and retro virus disease therapy
AUTHOR: **Ecker D J;** Bruice T W; Vickers T
CORPORATE SOURCE: Carlsbad, CA, USA.
PATENT ASSIGNEE: Isis-Pharm. 1999
PATENT NUMBER: US 5874564 PATENT DATE: 990223 WPI ACCESSION NO.: 99-180068 (9915)
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ABSTRACT: Oligonucleotides (or their analogs) able to mimic the secondary or tertiary structure of RNA molecules, especially mRNA, are claimed. Specific oligonucleotides which mimic the HIV virus trans-acting responsive element (TAR) are claimed. Also claimed are oligonucleotides of 8-50 residues containing the 4 disclosed RNA sequences with virucide activity. The RNA mimicry oligonucleotides mimic particular strands of RNA, especially mRNA, containing secondary structures important for RNA/protein interactions. The interaction of proteins with mimic molecules minimizes the interactions of proteins with regulatory RNA. A 2'-O-methyl oligonucleotide analog 29-mer forms a truncated HIV virus TAR **stem/loop** structure that binds to the tat peptide in vitro. This oligonucleotide showed high inhibition of HIV virus gene expression. The oligonucleotides are useful for gene expression modification and in gene therapy of virus and retro virus infections e.g. AIDS. The oligonucleotides can also be used as RNA probes in diagnosis and research. (21pp)
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